Perampanel (Fycompa)

Criteria for Use

June 2016

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or http://vaww.pbm.va.gov for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive perampanel.*

☐ Preexisting aggression, hostility, irritability, anger, homicidal ideation and threats that is uncontrolled/untreated

☐ Planned use as monotherapy

☐ Patient has severe hepatic impairment (Child Pugh Class C)

☐ Patient has severe renal impairment (CrCL 10-30 ml/min) or is on hemodialysis

Inclusion Criteria *The answers to the following must be fulfilled in order to meet criteria.*

☐ Medication management by a VA Neurologist or in consultation with one.

AND

☐ The patient has had inadequate response, intolerable side effects, or contraindication to two formulary antiepileptic medications for partial seizures, such as: carbamazepine, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, divalproex sodium, topiramate, or zonisamide or for primarily generalized seizures; lamotrigine, levetiracetam, topiramate, valproate or zonisamide

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For women of childbearing potential

Perampanel is Category C. Adverse events were observed in animal reproduction studies. Available information related to use in pregnancy is limited; if inadvertent exposure occurs during pregnancy, close monitoring of the mother and fetus/newborn is recommended.

Dosage and Administration

Dosing in the absence of enzyme-inducing antiepileptic drugs (AEDs)

- Starting dose: 2 mg once daily orally at bedtime
- May increase dose based on clinical response and tolerability by increments of 2 mg once daily no more frequently than at weekly intervals. A slower titration rate may assist in identification of potential side effects such as aggression.
- Recommended maintenance dose: Partial-Onset Seizures – 8 to 12 mg once daily at bedtime;

  Primary Generalized Tonic-Clonic Seizures – 8 mg once daily at bedtime

Dosing in the presence of enzyme-inducing antiepileptic drugs (AEDs)

- Enzyme-inducing AEDs, including phenytoin, carbamazepine, and oxcarbazepine, cause a 50-67% reduction in perampanel plasma levels.
- In patients receiving concomitant enzyme-inducing AEDs, the recommended starting dosage of perampanel is 4 mg once daily taken orally at bedtime.
- Increase dosage by increments of 2 mg once daily no more frequently than at weekly intervals. A maintenance dose has not been established in clinical trials. The highest dose studied in patients on concomitant enzyme-inducing AEDs was 12 mg once daily.

Issues for Consideration

- Perampanel is the only antiepileptic drug to have a black box warning due to its association with serious or life-threatening psychiatric and behavioral adverse reactions including aggression, hostility, irritability, anger and homicidal ideation and threats. These reactions occurred in patients with and without prior psychiatric history, prior aggressive behavior, or concomitant use of medications associated with hostility and aggression.
- Antiepileptic drugs (AEDs), including perampanel, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Monitor patients treated with any AED for any indication for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior
- Perampanel is affected by strong inducers of the CYP3A4 system. Agents that are strong inducers (rifampin, St. John's wort.) should not be used. The effectiveness of hormonal contraceptives containing levonorgestrel may decrease with 12 mg once daily dose of perampanel. Administration of perampanel and enzyme inducing antiepileptics may compromise the efficacy of perampanel.

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